Keytruda® (pembrolizumab) plus Padcev® (enfortumab vedotin-ejfv) – New indication

- On April 3, 2023, the FDA announced the approval of Merck's Keytruda (pembrolizumab) plus Astellas Pharma's Padcev (enfortumab vedotin-ejfv), for the treatment of adult patients with locally advanced or metastatic urothelial carcinoma who are not eligible for cisplatin-containing chemotherapy.
    - This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.
- Both Keytruda and Padcev are approved as single agents for other uses in urothelial carcinoma. Additionally, Keytruda is approved across over 30 other indications and uses. Refer to the Keytruda and Padcev drug labels for a complete list of indications and uses.
- The approval of Keytruda plus Padcev for the new indication was based on EV-103/ KEYNOTE-869, an open-label, multi-cohort study in 121 patients with locally advanced or metastatic urothelial cancer who were ineligible for cisplatin-containing chemotherapy. The dose escalation cohort and Cohort A were single-arm cohorts treating patients with Keytruda plus Padcev while patients on Cohort K were randomized to either the combination or to Padcev alone. The major efficacy measures were objective response rate (ORR) and duration of response (DOR).
    - The ORR was 68% (95% CI: 58.7, 76.0).
    - The median DOR for the dose escalation cohort + Cohort A was 22.1 months (range: 1.0+ to 46.3+) and for Cohort K was not reached (range: 1.2 to 24.1+).
- Padcev carries a boxed warning for serious skin reactions.
- The most common adverse reactions, including laboratory abnormalities (≥ 20%), with Keytruda plus Padcev use were increased glucose, increased aspartate aminotransferase, rash, decreased hemoglobin, increased creatinine, peripheral neuropathy, decreased lymphocytes, fatigue, increased alanine aminotransferase, decreased sodium, increased lipase, decreased albumin, alopecia, decreased phosphate, decreased weight, diarrhea, pruritus, decreased appetite, nausea, dysgeusia, decreased potassium, decreased neutrophils, urinary tract infection, constipation, increased potassium, increased calcium, peripheral edema, dry eye, dizziness, arthralgia, and dry skin.
- When used in combination with Padcev, the recommended dose of Keytruda for the treatment of urothelial carcinoma is 200 mg every 3 weeks or 400 mg every 6 weeks administered via intravenous (IV) infusion until disease progression, unacceptable toxicity, or up to 24 months.
    - Keytruda should be administered after Padcev when given on the same day.
    - Refer to the Keytruda drug label for dosing for all its other indications.
- When used in combination with Keytruda, the recommended dose of Padcev for the treatment of urothelial carcinoma is 1.25 mg/kg (up to a maximum of 125 mg for patients ≥ 100 kg) administered as an IV infusion on days 1 and 8 of a 21-day cycle until disease progression or unacceptable toxicity.

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— Refer to the Padcev drug label for its use as a single agent for urothelial carcinoma.